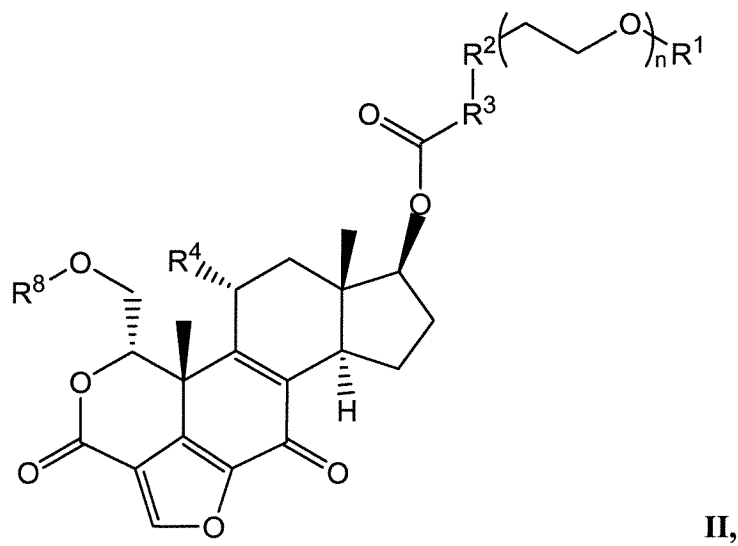
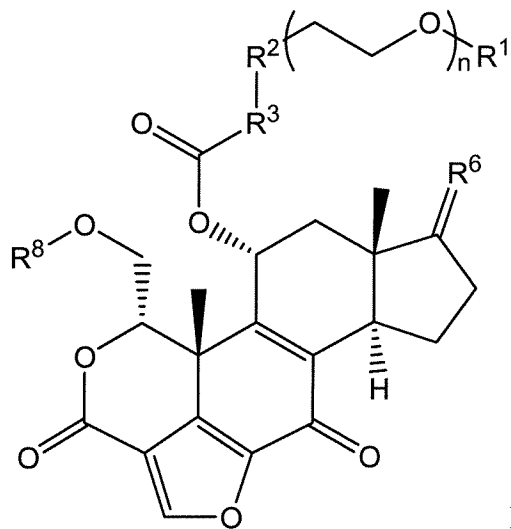
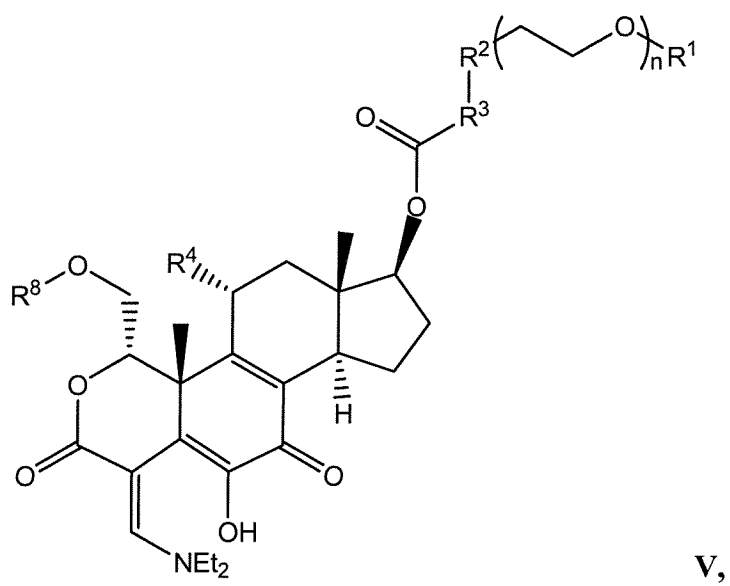
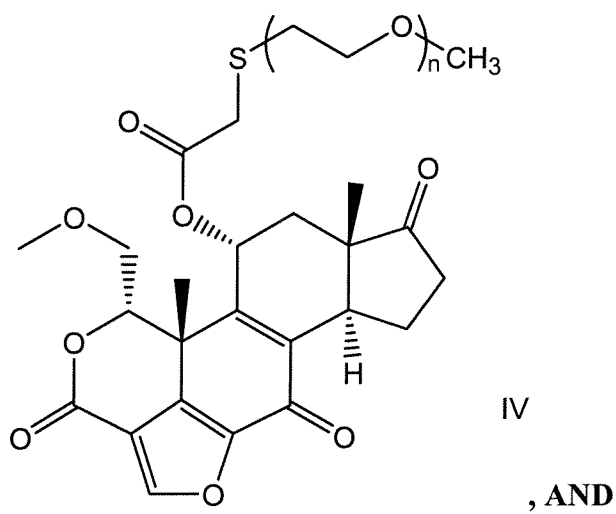
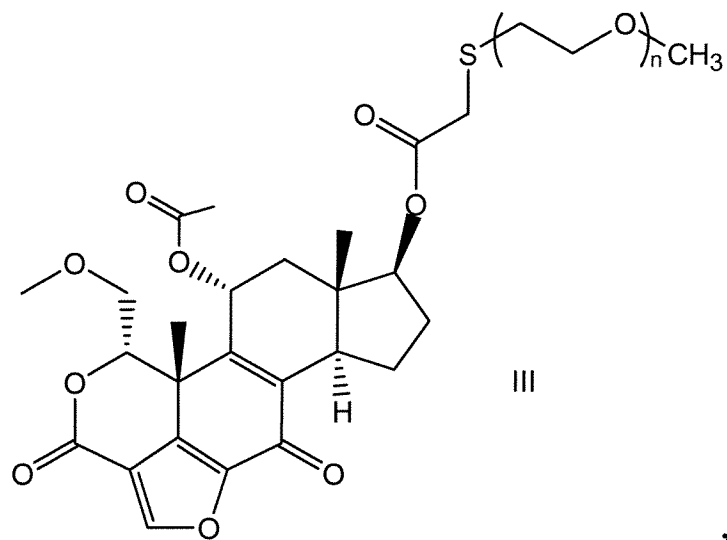


# **Listing of Claims:**

This listing of claims will replace all prior versions and listing of claims in this application:

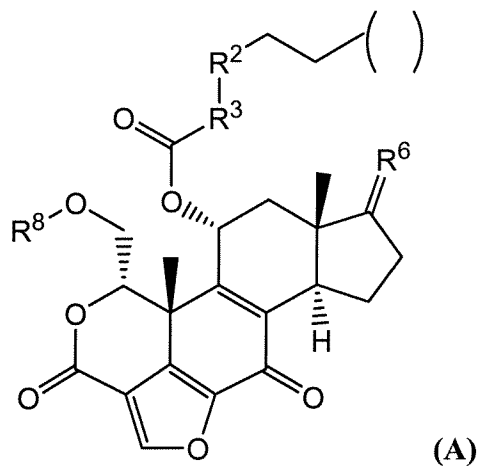
1. (Previously Presented) A water-soluble drug-polymer conjugate selected from a conjugate of formula I, II, III, IV and V:



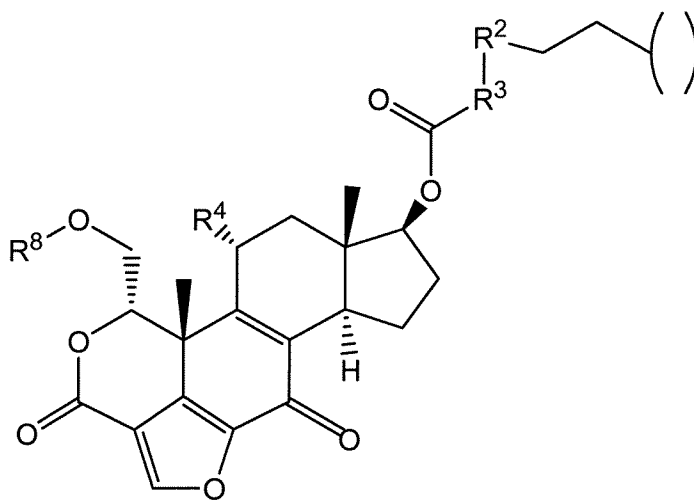


wherein

$R^1$  is alkyl, a drug-polymer conjugate of formula (A) or a drug-polymer conjugate of formula (B):



(A)



(B);

$R^2$  is  $-O-$ ,  $-NH-$ , or  $-S-$ ;

$R^3$  is alkyl, a cycloalkyl, or aryl;

$R^4$  is  $H$ ,  $=O$ ,  $-O-COC_4H_9$ , or  $OR^7$ ;

$R^6$  is  $=O$  or  $OR^7$ ;

R<sup>7</sup> is H, COR<sup>9</sup> or alkyl;

R<sup>8</sup> is alkyl or H;

R<sup>9</sup> is alkyl, H, aryl, or -CH<sub>2</sub>Ar; and

n is 1-1000.

2. (Original) A pharmaceutical composition comprising the water-soluble drug-polymer conjugate of claim 1 and a pharmaceutically acceptable carrier.

3. (Currently Amended) A method for treating ~~or inhibiting~~ a pathological condition or disorder mediated in a mammal comprising providing to said mammal an effective amount of a water-soluble drug-polymer conjugate of claim 1.

4. (Original) A method of claim 3 wherein the effective amount of the water-soluble drug-polymer is 10 to 1000 mg/kg.

5. (Original) A method of claim 3 wherein the effective amount of the water-soluble drug-polymer is 0.5 to 10 mg/kg.

6. (Currently Amended) A method of claim 3 wherein treating ~~or inhibiting~~ comprises inhibition of PI3 kinase.

7. (Currently Amended) A method of claim 3 wherein treating ~~or inhibiting~~ comprises inhibition of TOR kinase.

8. (Original) A method of claim 3 wherein the pathological condition is non-small cell lung cancer.

9. (Withdrawn) A method of claim 3 wherein the pathological condition is brain cancer, ischaemic heart disease, restenosis, inflammation, platelet aggregation, sclerosis, respiratory disorder, HIV and bone resorption.

10. (Withdrawn) A method of claim 3 wherein providing an effective amount is alone or in combination with other agents that modulate growth factor signaling, cytokine response, and cell cycle control.

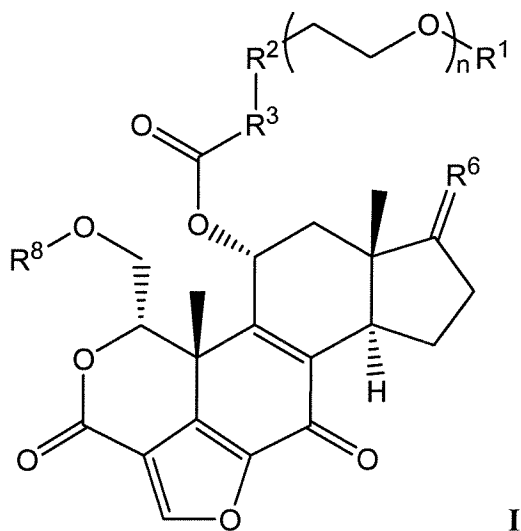
11. (Withdrawn) A method of claim 10 wherein the agent is interferon- $\alpha$ .

12. (Withdrawn) A method of claim 10 wherein the agent is pegylated rapamycin.

13. (Withdrawn) A method of claim 10 wherein the agent is a cytotoxic.

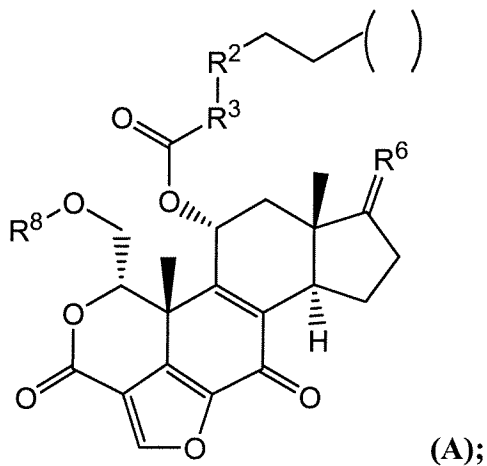
14. (Withdrawn) A water-soluble drug-polymer conjugate having the structure of formula

I



wherein:

R<sup>1</sup> is alkyl, or a drug-polymer conjugate of formula (A)



$R^2$  is -O-, -NH-, or -S-;

$R^3$  is alkyl, a cycloalkyl, or aryl;

$R^6$  is =O or  $OR^7$ ;

$R^7$  is H,  $COR^9$  or alkyl;

$R^8$  is alkyl or H;

$R^9$  is alkyl, H, aryl, or  $-CH_2Ar$ ; and

n is 1-1000.

15. (Withdrawn) The water-soluble drug-polymer conjugate of claim 14 wherein n is 250 – 400.

16. (Withdrawn) The water-soluble drug-polymer conjugate of claim 14 wherein n is 50 – 150.

17. (Withdrawn) The water-soluble drug-polymer conjugate of claim 14 wherein the molecular weight of polymer is from about 400 to about 80,000.

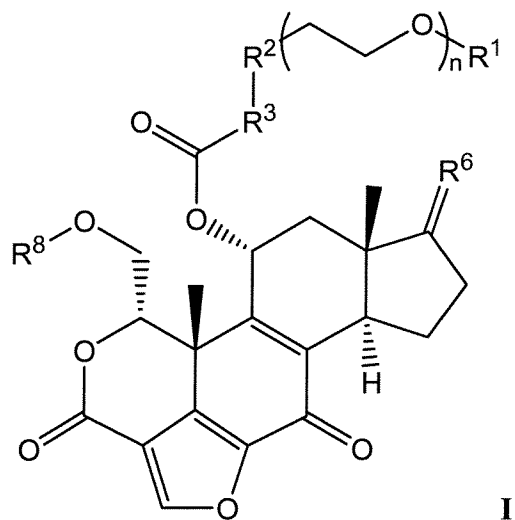
18. (Withdrawn) The water-soluble drug-polymer conjugate of claim 14 wherein the molecular weight of polymer from about 1000 to about 8000.

19. (Withdrawn) The water-soluble drug-polymer conjugate of claim 14 wherein the molecular weight of polymer is from about 4000 to about 6000.

20. (Withdrawn) A pharmaceutical composition comprising the water-soluble drug-polymer conjugate of claim 14 and a pharmaceutically acceptable carrier.

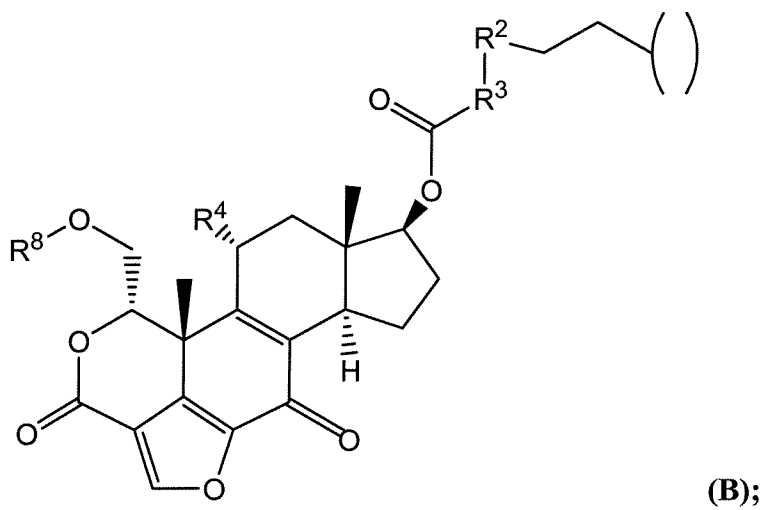
21. (Withdrawn-Currently Amended) A method for treating ~~or inhibiting~~ a pathological condition or disorder mediated in a mammal comprising providing to said mammal an effective amount of a water-soluble drug-polymer conjugate of claim 14.

22. (Withdrawn) A method of claim 21 wherein the effective amount of the water-soluble drug-polymer is 10 to 1000 mg/kg.
23. (Withdrawn) A method of claim 21 wherein the effective amount of the water-soluble drug-polymer is 0.5 to 10 mg/kg.
24. (Withdrawn-Currently Amended) A method of claim 21 wherein treating ~~or inhibiting~~ comprises inhibition of PI3 kinase.
25. (Withdrawn-Currently Amended) A method of claim 21 wherein treating ~~or inhibiting~~ comprises inhibition of TOR kinase.
26. (Withdrawn) A method of claim 21 wherein the pathological condition is non-small cell lung cancer.
27. (Withdrawn) A method of claim 21 wherein the pathological condition is brain cancer, ischaemic heart disease, restenosis, inflammation, platelet aggregation, sclerosis, respiratory disorder, HIV and bone resorption.
28. (Withdrawn) A method of claim 21 wherein providing an effective amount is alone or in combination with other agents that modulate growth factor signaling, cytokine response, and cell cycle control.
29. (Withdrawn) A method of claim 28 wherein the agent is interferon- $\alpha$ .
30. (Withdrawn) A method of claim 28 wherein the agent is pegylated rapamycin.
31. (Withdrawn) A method of claim 28 wherein the agent is a cytotoxic.
32. (Withdrawn) A water-soluble drug-polymer conjugate having the structure of formula I:



wherein:

$R^1$  is alkyl, or a drug-polymer conjugate of formula (B)



$R^2$  is -O-, -NH-, or -S-;

$R^3$  is alkyl, a cycloalkyl, or aryl;

$R^4$  is H, =O, -O-COC<sub>4</sub>H<sub>9</sub>, or OR<sup>7</sup>;

$R^7$  is H, COR<sup>9</sup> or alkyl;



R<sup>8</sup> is alkyl or H;

R<sup>9</sup> is alkyl, H, aryl, or -CH<sub>2</sub>Ar; and

n is 1-1000.

33. (Withdrawn) The water-soluble drug-polymer conjugate of claim 32 wherein n is 250 – 400.

34. (Withdrawn) The water-soluble drug-polymer conjugate of claim 32 wherein n is 50 – 150.

35. (Withdrawn) The water-soluble drug-polymer conjugate of claim 32 wherein the molecular weight of polymer is from about 400 to about 80,000.

36. (Withdrawn) The water-soluble drug-polymer conjugate of claim 32 wherein the molecular weight of polymer is from about 1000 to about 8000.

37. (Withdrawn) The water-soluble drug-polymer conjugate of claim 32 wherein the molecular weight of polymer is from about 4000 to about 6000.

38. (Withdrawn) A pharmaceutical composition comprising the water-soluble drug-polymer conjugate of claim 32 and a pharmaceutically acceptable carrier.

39. (Withdrawn-Currently Amended) A method for treating ~~or inhibiting~~ a pathological condition or disorder mediated in a mammal comprising providing to said mammal an effective amount of a water-soluble drug-polymer conjugate of claim 32.

40. (Withdrawn) A method of claim 39 wherein the effective amount of the water-soluble drug-polymer is 10 to 1000 mg/kg.

41. (Withdrawn) A method of claim 39 wherein the effective amount of the water-soluble drug-polymer is 0.5 to 10 mg/kg.

42. (Withdrawn-Currently Amended) A method of claim 39 wherein treating ~~or inhibiting~~ comprises inhibition of PI3 kinase.

43. (Withdrawn-Currently Amended) A method of claim 39 wherein treating ~~or inhibiting~~ comprises inhibition of TOR kinase.

44. (Withdrawn) A method of claim 39 wherein the pathological condition is non-small cell lung cancer.

45. (Withdrawn) A method of claim 39 wherein the pathological condition is brain cancer, ischaemic heart disease, restenosis, inflammation, platelet aggregation, sclerosis, respiratory disorder, HIV and bone resorption.

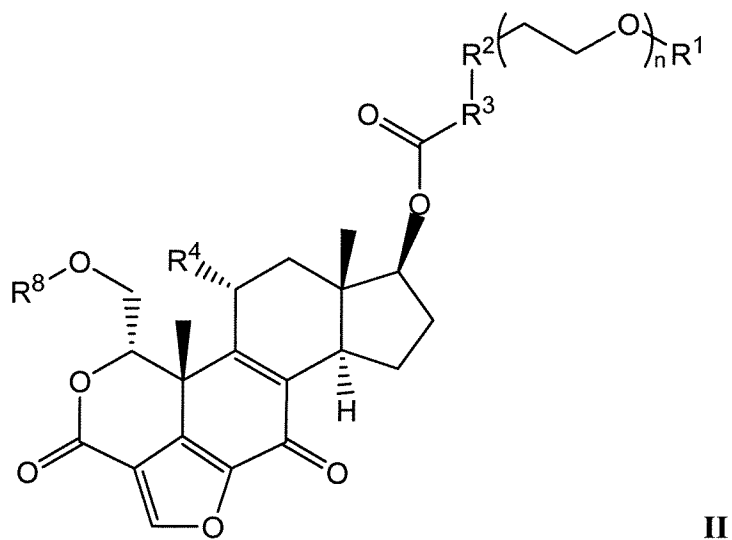
46. (Withdrawn) A method of claim 39 wherein providing an effective amount is alone or in combination with other agents that modulate growth factor signaling, cytokine response, and cell cycle control.

47. (Withdrawn) A method of claim 46 wherein the agent is interferon- $\alpha$ .

48. (Withdrawn) A method of claim 46 wherein the agent is pegylated rapamycin.

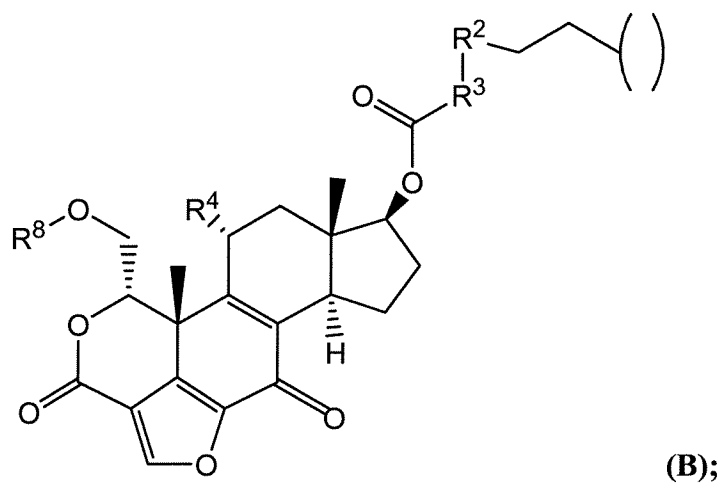
49. (Withdrawn) A method of claim 46 wherein the agent is a cytotoxic.

50. (Withdrawn) A water-soluble drug-polymer conjugate having the structure of formula II



wherein:

$R^1$  is alkyl, or a drug-polymer conjugate of formula (B)



$R^2$  is -O-, -NH-, or -S-;

$R^3$  is alkyl, a cycloalkyl, or aryl;

$R^4$  is H, =O, -O-COC<sub>4</sub>H<sub>9</sub>, or OR<sup>7</sup>;

$R^7$  is H, COR<sup>9</sup> or alkyl;

R<sup>8</sup> is alkyl or H;

R<sup>9</sup> is alkyl, H, aryl, or -CH<sub>2</sub>Ar; and

n is 1-1000.

51. (Withdrawn) The water-soluble drug-polymer conjugate of claim 50 wherein n is 250 – 400.

52. (Withdrawn) The water-soluble drug-polymer conjugate of claim 50 wherein n is 50 – 150.

53. (Withdrawn) The water-soluble drug-polymer conjugate of claim 50 wherein the molecular weight of polymer is from about 400 to about 80,000.

54. (Withdrawn) The water-soluble drug-polymer conjugate of claim 50 wherein the molecular weight of polymer is from about 1000 to about 8000.

55. (Withdrawn) The water-soluble drug-polymer conjugate of claim 50 wherein the molecular weight of polymer is from about 4000 to about 6000.

56. (Withdrawn) A pharmaceutical composition comprising the water-soluble drug-polymer conjugate of claim 50 and a pharmaceutically acceptable carrier.

57. (Withdrawn-Currently Amended) A method for treating ~~or inhibiting~~ a pathological condition or disorder mediated in a mammal comprising providing to said mammal an effective amount of a water-soluble drug-polymer conjugate of claim 50.

58. (Withdrawn) A method of claim 57 wherein the effective amount of the water-soluble drug-polymer is 10 to 1000 mg/kg.

59. (Withdrawn) A method of claim 57 wherein the effective amount of the water-soluble drug-polymer is 0.5 to 10 mg/kg.

60. (Withdrawn-Currently Amended) A method of claim 57 wherein treating ~~or inhibiting~~ comprises inhibition of PI3 kinase.

61. (Withdrawn-Currently Amended) A method of claim 57 wherein treating ~~or inhibiting~~ comprises inhibition of TOR kinase.

62. (Withdrawn) A method of claim 57 wherein the pathological condition is non-small cell lung cancer.

63. (Withdrawn) A method of claim 57 wherein the pathological condition is brain cancer, ischaemic heart disease, restenosis, inflammation, platelet aggregation, sclerosis, respiratory disorder, HIV and bone resorption.

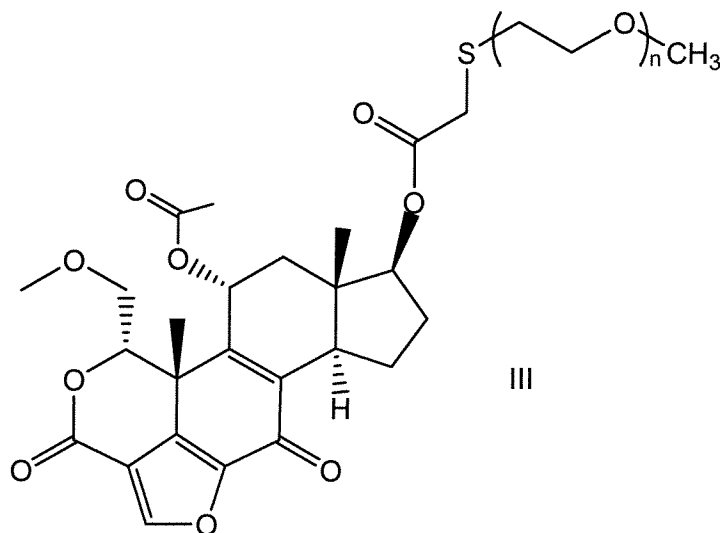
64. (Withdrawn) A method of claim 57 wherein providing an effective amount is alone or in combination with other agents that modulate growth factor signaling, cytokine response, and cell cycle control.

65. (Withdrawn) A method of claim 64 wherein the agent is interferon- $\alpha$ .

66. (Withdrawn) A method of claim 64 wherein the agent is pegylated rapamycin.

67. (Withdrawn) A method of claim 64 wherein the agent is a cytotoxic.

68. (Original) A water-soluble drug-polymer conjugate having the structure of formula III:



n is 1-1000.

69. (Original) The water-soluble drug-polymer conjugate of claim 68 wherein n is 250-400.

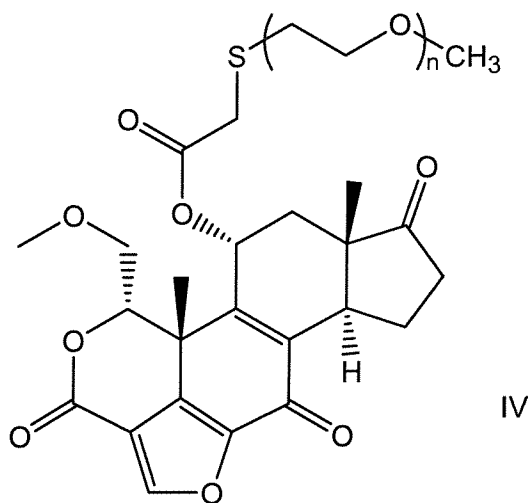
70. (Original) The water-soluble drug-polymer conjugate of claim 68 wherein n is 50-150.

71. (Original) The water-soluble drug-polymer conjugate of claim 68 wherein the molecular weight of polymer is from about 400 to about 80,000.

72. (Original) The water-soluble drug-polymer conjugate of claim 68 wherein the molecular weight of polymer is from about 1000 to about 8000.

73. (Original) The water-soluble drug-polymer conjugate of claim 68 wherein the molecular weight of polymer is from about 4000 to about 6000.

74. (Withdrawn) A water-soluble drug-polymer conjugate having the structure of formula IV:



wherein n = 1-1000.

75. (Withdrawn) The water-soluble drug-polymer conjugate of claim 74 wherein n is 250 – 400.

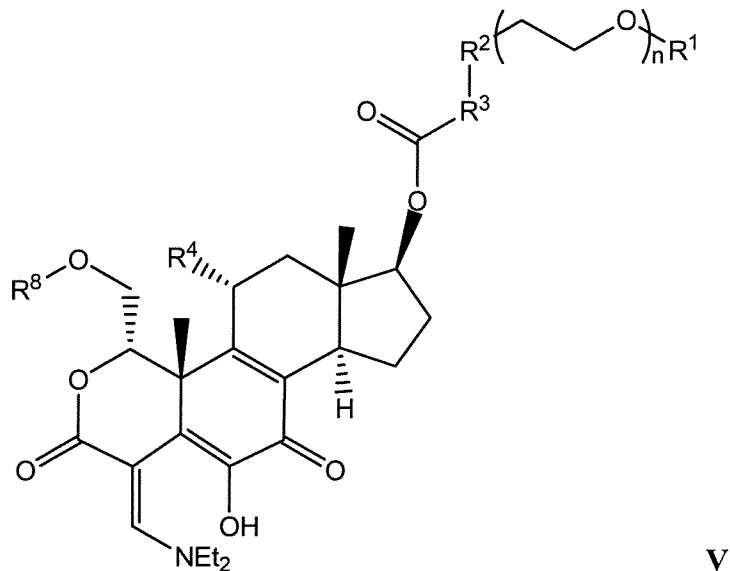
76. (Withdrawn) The water-soluble drug-polymer conjugate of claim 74 wherein n is 50 – 150.

77. (Withdrawn) The water-soluble drug-polymer conjugate of claim 74 wherein the molecular weight of polymer is from about 400 to about 80,000.

78. (Withdrawn) The water-soluble drug-polymer conjugate of claim 74 wherein the molecular weight of polymer is from about 1000 to about 8000.
79. (Withdrawn) The water-soluble drug-polymer conjugate of claim 74 wherein the molecular weight of polymer is from about 4000 to about 6000.
80. (Withdrawn) A pharmaceutical composition comprising the water-soluble drug-polymer conjugate of claim 74 and a pharmaceutically acceptable carrier.
81. (Withdrawn-Currently Amended) A method for treating ~~or inhibiting~~ a pathological condition or disorder mediated in a mammal comprising providing to said mammal an effective amount of a water-soluble drug-polymer conjugate of claim 74.
82. (Withdrawn) A method of claim 81 wherein the effective amount of the water-soluble drug-polymer is 10 to 1000 mg/kg.
83. (Withdrawn) A method of claim 81 wherein the effective amount of the water-soluble drug-polymer is 0.5 to 10 mg/kg.
84. (Withdrawn-Currently Amended) A method of claim 81 wherein treating ~~or inhibiting~~ comprises inhibition of PI3 kinase.
85. (Withdrawn-Currently Amended) A method of claim 81 wherein treating ~~or inhibiting~~ comprises inhibition of TOR kinase.
86. (Withdrawn) A method of claim 81 wherein the pathological condition is non-small cell lung cancer.
87. (Withdrawn) A method of claim 81 wherein the pathological condition is brain cancer, ischaemic heart disease, restenosis, inflammation, platelet aggregation, sclerosis, respiratory disorder, HIV and bone resorption.
88. (Withdrawn) A method of claim 81 wherein providing an effective amount is alone or in combination with other agents that modulate growth factor signaling, cytokine response, and cell cycle control.
89. (Withdrawn) A method of claim 88 wherein the agent is interferon- $\alpha$ .
90. (Withdrawn) A method of claim 88 wherein the agent is pegylated rapamycin.
91. (Withdrawn) A method of claim 88 wherein the agent is a cytotoxic.
92. (Withdrawn) A process for the preparation of a water-soluble drug-polymer conjugate of claim 68 comprising:

- a. adding a solvent to 17-dihydro-17-(1-iodoacetyl)-wortmannin to obtain a solution;
- b. adding a tertiary amine or sodium bicarbonate to the solution;
- c. adding mPEG-sulphydryl 5000 to the solution of step (b);
- d. stirring the solution of step (c) for 30 minutes;
- e. adding ether to the stirred solution;
- f. collecting the solid; and
- g. washing the collected solid with ether to obtain the pegylated wortmannin derivative.

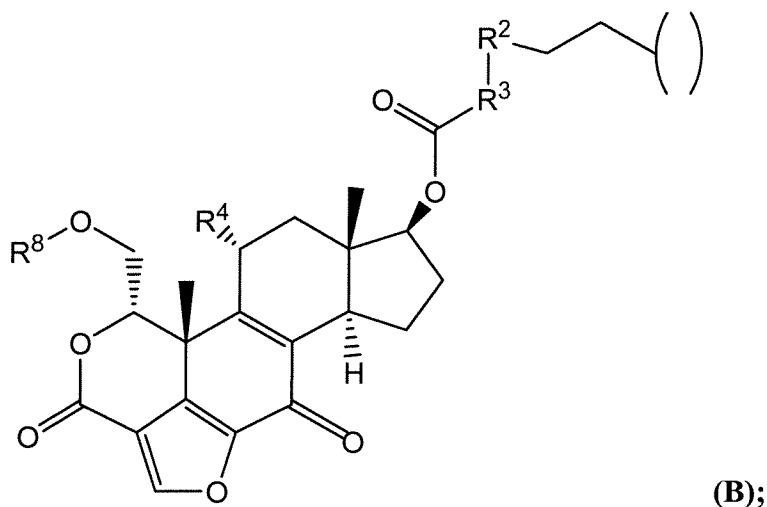
93. (Withdrawn) A water-soluble drug-polymer conjugate having the structure of formula V:



wherein:

$R^1$  is alkyl, or a drug-polymer conjugate of a single non-repeating formula (V)





$R^2$  is -O-, -NH-, or -S-;

$R^3$  is alkyl, a cycloalkyl, or aryl;

$R^4$  is H, =O, -O-COC<sub>4</sub>H<sub>9</sub>, or OR<sup>7</sup>;

$R^7$  is H, COR<sup>9</sup> or alkyl;

$R^8$  is alkyl or H;

$R^9$  is alkyl, H, aryl, or -CH<sub>2</sub>Ar; and

$n$  is 1-1000.

94. (Withdrawn) A process for the preparation of the compound of claim 93 comprising addition of an amine to a compound of claim 50 to obtain a compound of claim 93.

95. (Withdrawn) A process of claim 94 wherein the amine comprises diethyl amine.

96. (Withdrawn) A process for the preparation of a water-soluble drug-polymer conjugate of claim 74 comprising:

- a) adding a solvent to 11-desacetyl-11-(1-iodoacetyl)-wortmannin to obtain a solution;

- b) adding a tertiary amine to the solution;
- c) adding mPEG-sulphydryl 5000 to the solution of step (b);
- d) stirring the solution of step (c) for 30 minutes;
- e) adding ether to the stirred solution;
- f) collecting the solid; and
- g) washing the collected solid with ether to obtain the pegylated wortmannin derivative, as disclosed.